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EXAMINER	
FORMAN, BETTY J	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary	Application No.	Applicant(s)	
	10/055,367	CASS, ANTHONY E.G.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *32-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☒ Claim(s) *10-12, 14, 22-24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 4 March 2004 in which claims 1, 24, 27,29, 32, 47-50 were amended and claims 9 and 21were canceled. All of the amendments have been thoroughly reviewed and entered.

The previous objections and rejections of Claims 1-30 in the Office Action dated 15 September are withdrawn in view of the amendments. The claims have been amended to introduce the limitations of canceled Claim 9 into independent Claim 1 thereby defining the sensing element of Claims 1-30 as a "polypeptide, or a fragment, truncation, domain, or concatenation thereof comprising at least a ligand binding site of the polypeptide".

The previous rejection of Claim 31 is maintained because the "biological sensing element" of the claim encompasses the array of Reed wherein the cell is a sensing element.

Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant rejections. New grounds for rejection necessitated by amendment are discussed.

Claims 1-31 are under prosecution.

Formalities

2. The listing of the claims is objected to because withdrawn claims 32-50 are incorrectly identified as "original" or "amended". The proper identifier for withdrawn claims is "withdrawn" as required by 37 C.F.R. 1.121.

Claim Objections

3. Claims 10-12, 14, 22-24 are objected to because of the following informalities:

a. Claims 10-12 improperly depend from Canceled Claim 9. For purposes of examination, the claims are interpreted as depending from Claim 1.

b. Claim 14 is objected to because it does not further limit Claim 1.

c. Claims 22-24 improperly depend from Canceled Claim 21. For purposes of examination, the claims are interpreted as depending from Claim 1.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-5, 10, 13-14, 20, 25-26, 28-31 are rejected under 35 U.S.C. 102(e) as being anticipated by Reed et al (U.S. Patent No. 6,492,143, filed 17 December 1998).

Regarding Claim 1, Reed et al disclose a detector array comprising one or more groups of broad specificity biological sensing elements and variants thereof discretely immobilized onto a solid support ("arrayed in microtiter plates", Column 34, lines 62-65) wherein the sensing element is a polypeptide fragment comprising a ligand binding site (Column 33, lines 27) wherein the sensing elements have attached thereto a detectable label (e.g. rhodopsin-tagged protein, Column 33, lines 4-48 and Column 16, lines 16-54) and (Column 32, line 50-Column 34, line 3).

Regarding Claim 2, Reed et al disclose the detector wherein there is at least one group (Column 34, lines 58-67).

Regarding Claim 3, Reed et al disclose the detector wherein there are from 2 to 50 groups (Column 34, lines 58-67).

Regarding Claim 4, Reed et al disclose the detector wherein the group consists of a biological sensing element and from 1 to 100 variants (Column 34, lines 58-67).

Regarding Claim 5, Reed et al disclose the detector wherein the group consists of a biological sensing element and from 5 to 25 variants (Column 34, lines 58-67).

Regarding Claim 10, Reed et al disclose the detector wherein the ligand binding site contains one or more cysteine residues (Example 1, e.g. Column 23, lines 5-11 and 39-44, Column 24, lines 5-9 and 38-42).

Regarding Claim 13, Reed et al disclose the detector wherein a variant is derived from a sensing element (i.e. odorant-binding protein) and differ is binding specificity (Column 34, line 58-Column 35, line 45).

Regarding Claim 14, Reed et al disclose the detector wherein the element is a polypeptide comprising a ligand binding site (Column 7, lines 42-58).

Regarding Claim 20, Reed et al disclose the detector wherein the label is susceptible to change upon ligand binding i.e. Ca^{+2} dependent signal is detected (Column 33, line 28-Column 34, line 3).

Regarding Claim 25, Reed et al disclose the detector wherein the label is a fluorophore i.e. FITC-coupled antibody probing rhodopsin (Column 33, line 4-20).

Regarding Claim 26, Reed et al disclose the detector wherein the label is a labeled probe i.e. FITC-coupled antibody probing rhodopsin (Column 33, line 4-20).

Regarding Claim 28, Reed et al disclose the detector wherein the sensing element is an odorant binding protein from a mammalian organ (Abstract).

Regarding Claim 29, Reed et al disclose the detector wherein the sensing element is a mammalian binding protein (Column 8, lines 52-55 and Example 1, Column 22, lines 15-17).

Regarding Claim 30, Reed et al disclose the detector wherein the sensing element is a human odorant binding protein (Column 8, lines 52-55).

Regarding Claim 31, Reed et al disclose a detector array comprising a plurality of discrete biological sensing elements immobilized onto a solid support wherein each sensing element has a ligand binding site capable of binding a broad range of structurally diverse ligands, the sensing element are provided in groups, each comprising at least one variant differing ligand binding from the element from which it was derived (Column 34, line 56-Column 35, line 45) and each sensing element and variant having a detectable label attached wherein the physical characteristics of the label being susceptible to change upon ligand binding i.e. Ca^{+2} dependent signal is detected (Column 33, line 28-Column 34, line 3).

Response to Arguments

6. Claims 1-30 have been amended to define the sensing element as a polypeptide or a fragment, truncation, domain or concatenation thereof. Claim 31 has not been amended and therefore the previous interpretation of the invention wherein the sensing element encompasses the cell of Reed et al stands.

Applicant argues that the teaching of Reed et al differs from the instant invention two ways 1) the receptors of Reed et al are not "discretely immobilized onto or within a solid

support, and 2) the receptors of Reed et al do not have attached thereto a detectable label. The arguments have been considered but are not found persuasive because Reed et al specifically teach 1) the sensing elements (i.e. clones expressing TM II-IV receptor) "arrayed in microtiter plates", Column 34, lines 62-65) and the polypeptide having a detectable label attached label (i.e. rhodopsin-tagged protein, Column 33, lines 4-48). Hence, Reed et al teach the detector array as claimed.

7. Claims 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Reed et al (U.S. Patent No. 6,492,143, filed 17 December 1998) as defined by Dal Monte et al (Chemical Senses, 1993, 18(6): 713-721).

Regarding Claims 6-8, Reed et al disclose a detector array comprising one or more groups of broad specificity biological sensing elements and variants thereof discretely immobilized onto a solid support ("arrayed in microtiter plates", Column 34, lines 62-65) wherein the sensing element is a polypeptide fragment comprising a ligand binding site (Column 33, lines 27) wherein the sensing elements have attached thereto a detectable label (e.g. rhodopsin-tagged protein, Column 33, lines 4-48 and Column 16, lines 16-54) and (Column 32, line 50-Column 34, line 3)wherein the sensing elements are human odorant-binding proteins (Column 8, lines 52-67) which Dal Monte et al define as being less than 50kDa (Abstract).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 11-12, 15-19 and 22-24are rejected under 35 U.S.C. 103(a) as being unpatentable over by Reed et al (U.S. Patent No. 6,492,143, filed 17 December 1998) in view of Hoffman et al (U.S. Patent No. 5,998,588, filed 30 August 1996).

Regarding Claims 11-12, 15-19 and 22-24, disclose a detector array comprising one or more groups of broad specificity biological sensing elements and variants thereof discretely immobilized onto a solid support ("arrayed in microtiter plates", Column 34, lines 62-65) wherein the sensing element is a polypeptide fragment comprising a ligand binding site (Column 33, lines 27) wherein the sensing elements have attached thereto a detectable label (e.g. rhodopsin-tagged protein, Column 33, lines 4-48 and Column 16, lines 16-54) and (Column 32, line 50-Column 34, line 3). Reed et al do not teach the ligand binding site is modified to contain cysteine residues or the variants contain from 1 to 5 or 2 to 4 points of difference from the element from which they were derived and which affects binding specificity. However, Hoffman et al teach a similar detector array wherein biological sensing elements are immobilized onto a solid support and have a label attached thereto wherein variants of the sensing elements being modified to contain cysteine residues and having between 2 to 4 amino acids difference binding elements wherein the differences affect binding specificity (Column 16, lines 10-58) wherein the label is attached to a cysteine residue within the binding site or at

different amino acid positions within the binding site (Column 11, line 61-Column 12, line 32; Column 16, lines 48-58 and Column 16, line 59-Column 17, line 41) wherein the binding site modifications provide the means for directing and controlling binding interactions (Column 2, lines 50-57). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the binding analysis of Reed et al by modifying the binding site to contain cysteine residues and labels to thereby direct, control and detect binding interactions as taught by Hoffman et al (Column 2, lines 50-57).

Response to Arguments

10. Applicant argues that Hoffman is distinct from the instant invention because Hoffman is concerned with labeling a sensing element to manipulate ligand binding while the instant invention is simply concerned with detection of ligand binding. In response to applicant's argument that Hoffman labels their receptor for a different purpose, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Furthermore, as stated above, Hoffman clearly provide motivation for combination of the teachings wherein they teach binding site modifications provide the means for directing and controlling binding interactions (Column 2, lines 50-57). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the binding analysis of Reed et al by modifying the binding site to contain cysteine residues and labels to thereby direct, control and detect binding interactions as taught by Hoffman et al (Column 2, lines 50-57).

Applicant argues that with instant invention, "Exposure to ligand results in a certain amount of ligand binding to the elements/variants, which is detected by a change in the characteristics of the label. The change in the characteristics of the label is brought about by ligand binding and not by the introduction of an external stimulus. Furthermore,

quantification of ligand binding is determined by a determination of the extent of the change in the characteristics of the label."

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., amount of ligand binding, change in label characteristics, quantification of binding via extent of label change) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, Applicant's arguments address functional applications/characteristics of the claimed detector array. Arguments regarding functionality are moot in view of the fact that claims drawn to a product/apparatus must be distinguished over the prior art in terms of structure, not function.

The courts have stated that claims drawn to an apparatus must be distinguished from the prior art in terms of structure rather than function see *In re Danly*, 263 F.2d 844, 847, 120 USPQ 528, 531 (CCPA1959). "[A]pparatus claims cover what a device is, not what a device does." Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525,1528 (Fed. Cir. 1990) (see MPEP, 2114).

Applicant argues that a combination of Reed et al and Hoffman et al would not work because one of ordinary skill would not have contemplated using the stimulus response system of Hoffman with the library-based assay of Reed because Hoffman requires attachment of the stimulus response component to the interactive molecule. Applicant's arguments has been considered but is not found persuasive. Applicant's assertions regarding the knowledge of one of ordinary skill in the art are not supported by any factual evidences. Therefore, the argument is not persuasive.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze,

346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, **inoperability of the prior art**, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. (see (MPEP 716.01(c).

Applicant further argues that a combination of the references, in contrast to the instant invention, would not allow detection of the quantity of bound ligand. The argument is not found persuasive because the claims are drawn to a detector array. As discussed above, the functional properties of the array are not claimed and would not distinguish over the structural properties disclosed in the prior art.

Applicant argues that the receptor of Reed is expressed in the cell and any modification of the binding site to include cysteine residues would require mutageneis prior to expression that may affect expression. Applicant's assertion regarding mutagenesis affecting expression is not found persuasive because it is not supported by any factual evidences but merely appears to be arguments of counsel. Therefore, the argument is not persuasive. Furthermore, the argument does not address limitations of the claims.

Applicant argues that Reed does not disclose attachment of a label to the expressed protein and hence introduction of cysteine residues would not advance the system of Reed. The argument has been considered but is not found persuasive because, as cited above, Reed clearly attaches a label to the polypeptide sensing element as claimed (Example 1 and Column 33, lines 4-18).

11. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over by Reed et al (U.S. Patent No. 6,492,143, filed 17 December 1998) Gold et al (U.S. Patent No. 6,242,246, filed 15 December 1997).

Regarding Claim 27, Reed et al disclose a detector array comprising one or more groups of broad specificity biological sensing elements and variants thereof discretely immobilized onto a solid support ("arrayed in microtiter plates", Column 34, lines 62-65) wherein the sensing element is a polypeptide fragment comprising a ligand binding site (Column 33, lines 27) wherein the sensing elements have attached thereto a detectable label (e.g. rhodopsin-tagged protein, Column 33, lines 4-48 and Column 16, lines 16-54) and (Column 32, line 50-Column 34, line 3) but they do not teach the label is a fluorescent probe selected from the claimed group. However, Gold et al teach a similar method comprising one or more groups of broad specificity biological sensing elements and variants thereof (Column 2, lines 27-37) discretely immobilized onto a solid support wherein the sensing elements have attached thereto a detectable label (Column 13, lines 37-59 and fig. 5) wherein the label is a fluorescent probe selected from the claimed group (Column 15, line 44-Column 16, line 45) and wherein the fluorescent probe provides for binding analysis in a position-specific and dynamic manner (Column 15, lines 60-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the fluorescent probes of Gold et al to the labeled sensing elements of Reed et al for the expected benefit of obtaining binding analysis in a position-specific and dynamic manner as taught by Gold et al (Column 15, lines 60-65).

Response to Arguments

12. Applicant argues that the receptor of Reed does not have a label attached and thus one of ordinary skill would not have considered using the fluorescent probes of Gold. The

argument has been considered but is not found persuasive because, as stated above, Reed clearly attaches a label to the polypeptide sensing element as claimed (Example 1 and Column 33, lines 4-18).

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Primary Examiner
Art Unit: 1634
May 10, 2004